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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,068	NG ET AL.	
	Examiner	Art Unit	
	J. E. ANGELL	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-71* is/are pending in the application.

4a) Of the above claim(s) *60-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/23/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 7/23/2010.

The amendment filed 7/23/2010 is acknowledged and has been entered.

Claims 53-71 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

1. Newly submitted claims 60-71 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 60-71 are drawn to the same invention and/or species as set forth in cancelled claims 10, 12-19, 22, 23, 47 which were withdrawn from consideration as being drawn to a non-elected invention or species in the Non-Final Office Action, as acknowledged by Applicant in their 7/23/2010 submission. Since new claims 60-71 directed to subject that was previously withdrawn from consideration, new claims 60-71 are hereby also withdrawn from consideration.

2. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 60-71 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 53-59 are examined herein.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 7/23/2010 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 53-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing HBV viral titer in a host organism comprising inhibiting the formation of a complex between hnRNP K **and the human HBV regulatory region identified in claim 8**, does not reasonably provide enablement for methods of reducing HBV viral load or treating HBV infection by reducing the formation of a complex between hnRNP K and **any regulatory region on the HBV genome**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The present claims are drawn to methods for reducing the load of or treating an HBV infection in a host organism comprising the administration of a nucleic acid compound that reduces the amount of hnRNP K which in turn reduces the formation of a complex between hnRNP K and **ANY** regulatory region of the HBV genome. The instant specification appears to disclose a single regulatory region of the HBV genome that forms a complex with HBV, that being the region that is the enhancer II regulatory region of the human Hepatitis B virus (e.g., see Examples 9-10, pages 36-38).

None of the reference of record or other teachings found in a search of the art provided any evidence of interaction between hnRNP K with any other regulatory regions of HBV. That is, there is no evidence of record that hnRNP K forms a complex with any other regulatory region of the HBV genome other than the regulatory region that is the enhancer II regulatory region of HBV. Furthermore, there is no evidence in the present application or in the art that indicates that hnRNP K interacts with any non-enhancer II regulatory region of HBV in such a manner that inhibiting such an interaction would result in the inhibition of viral replication or otherwise act to reduce viral titer or effect a treatment for the viral infection.

3. Claims 53-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

4. The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

The present claims are drawn to methods for reducing the load of or treating an infection by a Hepatitis B virus (HBV), in a host organism comprising the administration of a nucleic acid compound that reduces the amount of hnRNP K which in turn reduces the formation of a complex between hnRNP K and any regulatory region of the HBV genome. Certain of the claims limit the compound to DNA or DNA aptamers (e.g., claims 58, 59). The claims are also drawn to methods wherein the desired result is achieved in vivo (e.g. in a hepatitis virus infected organism as in claims 53-58). Thus, the claims are generally drawn to method for the reducing

the load of, or treating infection by HBV in a host organism through the administration of any nucleic acid compound that, either directly or indirectly, reduces the amount of hnRNP K, thereby reducing the formation of a complex between hnRNP K and a regulatory region in the hepatitis B viral genome.

The claims are rejected on two grounds:

First, the claims are rejected as lacking adequate support for the inhibition of complex formation between hnRNP K and any regulatory region of the Hepatitis B virus genome.

None of the prior art of record, the present application, or other teachings found in a search of the art provided any evidence of interaction between hnRNP K with any regulatory regions of the human HBV other than the enhancer II regulatory region. That is, the only regulatory region of the HBV genome that was found to form a complex with hnRNP K is the enhancer II regulatory region. There is no evidence of record that hnRNP K forms a complex with any other regulatory region of the HBV genome.

Further, the application also fails to specifically identify any particular sequence or structure in such regulatory regions (i.e., the regulatory regions other than the enhancer II regulatory region) that could be considered to correspond to the ability to form complexes with hnRNP K. While the application identifies the enhancer II domain of human HBV as forming such a complex, the application nowhere indicates what specific characteristics of this domain are targeted by hnRNP K or enable the domain to bind hnRNP K such that those in the art may be able to correlate the presence of such sequences or structures in other HBV regulatory regions with the ability to form the target complexes.

In view of the lack of identification of other HBV genomic regulatory regions that interact with hnRNP K, the claims are rejected as lacking adequate descriptive support for the claimed method to inhibit the formation of a complex between hnRNP K and any regulatory region other than the enhancer II region the of the HBV genome. That is, the disclosure provides support for inhibiting the formation of a complex between hnRNP K and the enhancer II regulatory region of the HBV genome but not any other regulatory region of the HBV genome.

Second, the claims are also rejected as lacking adequate descriptive support for the elected nucleic acid compounds that may be administered to effect the reduction of the hnRNP K viral regulatory region complex formation.

The claims encompass nucleic acid compounds that are and that reduce the amount of hnRNP K in a cell, thereby reducing complex formation between hnRNP K and a regulatory region of the HBV genome. It is noted that the elected species is DNA and the nucleic acid compounds which are RNA have been withdrawn from consideration.

However, the specification provides only two examples of compounds that appear to reduce the amount of hnRNP K and thus be able to interfere with the complex formation, but the two types of compounds which are disclosed are: (1) anti-EGFR antibody, and (2) siRNA duplex against hnRNP K (see, pages 30-32). The specification does not appear to disclose a single DNA nucleic acid molecule, much less a DNA aptamer, that reduces the amount of hnRNP K in a cell. Furthermore, a search of the prior art did not identify a single DNA molecule (including DNA aptamer) that reduces the amount of hnRNP K in a cell. Therefore, at the time the invention was

made there is no evidence that a even a single specific DNA molecule that could reduce the amount of hnRNP K in a cell had been identified either in the prior art or in the specification.

Claim 58 and 59 specify that the nucleic acid compound that is administered is a DNA molecule or an aptamer, respectively. However, as indicated above, the application and prior art provide no examples of compounds of DNA generally or any specific DNA aptamers that achieve the desired functions (reducing the amount of hnRNP K in a cell). Nor does the application provide any guidance as to what structures/DNA sequences may correlate with utility in the claimed methods. It is noted that the art indicates that methods for the identification of aptamers that perform certain binding functions are known. See e.g., Ulrich et al. (Braz J Med Biol Res 34:295-300; previously cited). However, the knowledge or provision of such methods fails to provide support for compounds that may be identified through their use. See e.g., University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886, at 1895. Moreover, even though the art indicates that aptamers that target extracellular ligands may avoid problems associated with other forms of therapeutic nucleic acids (see e.g., Pestourie et al., Biochemie 87:921-30, at page 922, right column; of record), the present application provides only one example of such a target (page 30, identifying the epidermal growth factor receptor- EGFR), and provides no examples of DNA molecules, including DNA aptamers, against this receptor. Such teachings therefore fail to provide descriptive support for the claimed methods as they fail to provide support for the nucleic acid compounds that may be used in the methods.

In view of the breadth of the claimed genus, the lack of specific examples and the general uncertainty as to what DNA molecules and compounds may eventually be identified as

compounds that perform the required function, the claims are rejected as lacking adequate descriptive support for the claimed genus.

Response to Arguments

5. Applicant's arguments filed 7/23/2010 have been fully considered but with respect to the pending rejections, they are not persuasive.

6. Applicant argues that the amendment should overcome the rejection of claims under 35 112, first paragraph (enablement). However, the amendment does not address the enablement rejection with respect to targeting ANY regulatory region of the HBV genome as described above. Therefore, Applicant's argument is not persuasive.

7. Applicant argues that Example 6 demonstrates 3 different siRNAs against hnRNP K which reduce the amount of hnRNP K in cells. In response to applicant's argument, it is noted that the features upon which applicant relies (i.e., siRNAs against hnRNP K) are not recited in the claims 53-58. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, the elected species is DNA, thus siRNAs are non-elected embodiments which are not being examined at this time.

8. Applicants argue that the production of antisense molecules was well within the knowledge of a skilled artisan and that DNA aptamers can be generated from random sequence library and only requires the hnRNP K protein in order to obtain aptamers via the SELEX process. In response, it is noted that not a single DNA molecule that can reduce the amount of hnRNP K was known at the time the invention was made. MPEP 2163 clearly indicates the written description requirement for a claimed genus may be satisfied through sufficient

description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP 2163 also specifically indicates that a "representative number of species" means that the species which are adequately described are representative of the entire genus. In the instant case there is no actual reduction to practice, no reduction to drawings, and no disclosure of relevant identifying characteristics (i.e., no description of actual structure or other physical and/or chemical properties) sufficient to show the applicant was in possession of the claimed genus. Furthermore, as previously indicated, the knowledge or provision of methods to identify compounds fails to provide support for compounds that may be identified through their use. See e.g., University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886, at 1895.

9. Therefore, Applicant's arguments are not persuasive.

Conclusion

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. ANGELL whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 7:00 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Low, can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. ANGELL/
Primary Examiner, Art Unit 1635